

*REMARKS/ARGUMENTS**The Pending Claims*

Claims 21, 60, and 70-85 are pending, which claims are directed to a polypeptide that comprises a particular amino acid sequence and binds with HIV gp120 under physiological conditions (claims 21 and 70-77), and a composition comprising the polypeptide and a carrier (claims 60 and 78-85).

Summary of the Office Action

The Office maintains and makes final the rejection of claims 21, 60, and 70-85 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description support. All other rejections have been withdrawn. Applicant requests reconsideration of this rejection.

Discussion of the Written Description Rejection

The Office maintains the rejection of claims 21, 60, and 70-85 as lacking written description support insofar as they recite a polypeptide comprising one of the four recited amino acid sequences “with up to 6 conservative or neutral amino acid substitutions.” The Office substantially repeats the reasoning for the rejection that was presented in the prior Office Action.

In response to Applicant’s previous arguments, the Office states that it disagrees with Applicant’s assessment as to whether the specification discloses the molecular determinants that modulate gp120 activity. The Office restates its prior allegations that the specification fails to provide sufficient guidance as to which amino acids of the sequences recited in the claims can tolerate substitution, and that amino acid substitutions allegedly can have unpredictable results. The Office further alleges that even conservative or neutral amino acid substitutions can abrogate polypeptide activity.

For these reasons discussed in detail below, the Office has failed to set forth a *prima facie* case in support of the Section 112 rejection. Furthermore, even if the Office presented sufficient evidence to establish a *prima facie* case, which it does not, the reasoning and evidence provided by the Applicant in this and earlier communications is sufficient to overcome the rejection.

A. *The Office Has Not Established a Prima Facie Case Under Section 112*

There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. *In re Wertheim*, 541 F.2d 257, 263, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976); *In re Marzocchi*, 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971) (emphasis added). Furthermore, “it is incumbent upon the Patent Office ...

to explain why it doubts the truth or accuracy of any statement in a supporting disclosure *and to back up assertions of its own with acceptable evidence or reasoning* which is inconsistent with the contested statement." *In re Marzocchi*, 439 F.2d at 224, 169 U.S.P.Q. at 370 (emphasis added). A general allegation of "unpredictability in the art" is not a sufficient reason to support a rejection for lack of adequate written description. *Id.* See also, *MPEP* § 2163.04

The Office bases its rejection on allegations that it is "well-documented" that single amino acid substitutions can have unpredictable effects on peptide activity, and that "even conservative or neutral amino acid substitutions can abrogate peptide activity" (Office Action dated June 2, 2005 at pp. 4, 5). However, *the Office provides no evidence or reasoning in support of these allegations*. In particular, the Office provides no authority or explanation as to why it believes conservative or neutral amino acid substitutions, which are commonly understood by those of ordinary skill in the art as not likely to affect the function of a polypeptide (see included Declaration of Carl Saxinger, Ph.D., ("Saxinger Declaration") at para. 3), would be likely to abrogate peptide activity in the context of the invention. Instead, the Office relies upon unsupported allegations as a basis for its rejection, improperly attempting to shift the burden of proof to the Applicant. For this reason alone, the Office fails to set forth a *prima facie* case in support of the Section 112 rejection.

Even if the Office provided evidence to support its allegations, which it does not, the Office fails to explain how such allegations support the claim rejections. For instance, the Office does not explain how the predictability of the art pertains to the written description requirement. Predictability is a matter related to enablement; it is not the legal standard or test for written description. Moreover, it is irrelevant even as to the improper standard of "predictability" whether any single amino acid substitution *can* change peptide activity as predictability does not require absolute certainty; rather, predictability bears upon whether something is *likely* to occur. The Office makes no comment as to whether conservative amino acid substitutions are *likely* to have an effect on peptide activity.

With respect to the allegation that the application provides no guidance as to conservative or neutral amino acid substitutions, the Applicant previously referenced specific guidance in the application. Yet, the Office fails to explain why such specific guidance is insufficient. Instead, the Office merely alleges that it disagrees with the Applicant's assessment of the application because amino acid substitutions can be unpredictable. Such is not the "acceptable reasoning" required to establish *prima facie* support for a rejection under Section 112.

The pertinent issue is whether one of ordinary skill would recognize that the Applicant was in possession of the claimed subject matter at the time the application was filed. *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). This

inquiry is conducted from the viewpoint of one who possesses the general knowledge available in the art, in this case, knowledge as to conservative or neutral amino acid substitutions. *Id.* The Office does not properly address this issue. Indeed, the Office ignores completely the general knowledge that was available in the art at the time the application was filed, and fails to give adequate weight to the disclosures of the application. As discussed below, the chemical and physical properties of amino acids were well-characterized prior to filing of the present application, and suitable substitutes for any given amino acid residue were known.

For the foregoing reasons, the Office has not set forth a *prima facie* case under Section 112 and the burden does not shift to the Applicant to respond to the rejection. Accordingly, the Section 112 rejection should be withdrawn for this reason alone.

B. The Claims Meet the Written Description Requirement of Section 112

Although the burden of proof has not shifted to the Applicant to overcome the ill-supported rejection, the Applicant has nevertheless provided sufficient reasons and evidence to do so in this and earlier communications to the Office. In this regard, the Applicant reasserts its prior arguments as to the Section 112 rejection, and provides the following additional comments.

The sole contention of the Office is that the application does not adequately describe the amino acid sequences of SEQ ID NOs: 12-15 with *up to six conservative or neutral amino acid substitutions*. Those of ordinary skill in the art understand the term “conservative or neutral amino acid substitution” as referring a substitution of one amino acid for another having similar chemical and physical properties (Saxinger Declaration at para. 3). The ordinarily-skilled artisan, in reading the claims and disclosure of the specification, is already armed with the knowledge of the physical and chemical properties of the amino acid residues that are available, and can readily discern which amino acids have similar chemical properties such that they would be suitable for substitution (Saxinger Declaration at para. 4). In fact, such physical properties and groupings are described in the specification (specification at p. 7, line 12 – p. 8, line 11).

Thus, an amino acid sequence containing one or more conservative substitutions retains chemical and physical properties similar to the amino acid sequence upon which it is based (Saxinger Declaration at paras. 5 and 6). Since the function of a peptide is based upon the physical and chemical properties of the amino acid residues, a conservatively substituted sequence is expected to retain the function of the sequence upon which it is based at least to some degree (Saxinger Declaration at para. 6).

In this regard, the sequences themselves provide the essential information required for one of ordinary skill in the art to envision conservative substitutions that retain the ability to

bind to gp120. The amino acid sequences recited in the claims provide a “blue-print” of chemical and physical properties required to provide the desired function. Given the “blue print” of chemical and physical properties, it is a minor matter for the ordinarily skilled artisan to substitute one amino acid residue for another with similar properties because the “blue print” tells which properties are needed. Similarly, without the “blue-print” of the amino acid sequences provided by the Applicant, the ordinarily-skilled artisan would not have any suggestion at all as to what properties are required.

Furthermore, this “blue-print” of physical and chemical properties is common to the unsubstituted sequence and any conservatively substituted sequence that is based upon the sequence. Thus, contrary to the Office’s allegations, the application and claims describe the invention according to specific physical and chemical properties that are common to all species of the genus, which properties are explicitly tied to function. For example, the claimed polypeptide comprising SEQ ID NO: 12 with up to six conservative or neutral amino acid sequences shares the common structural motif defined by the physical and chemical properties of its sequence, which properties are common to the unsubstituted sequence and any conservatively substituted sequence based on SEQ ID NO: 12. Furthermore, the common physical and chemical properties are linked to the claimed function (e.g., gp120 binding). The courts have held such a description to meet the requirements of Section 112. *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002).

While the foregoing is sufficient to meet the requirements of Section 112, the present application provides even more guidance with respect to the claimed sequences. For instance, the Examples provided in the application demonstrate not only that the claimed sequences bind gp120, but that particular portions of the claimed sequences bind gp120 to a greater or lesser degree, or not at all (Saxinger Declaration at paras. 7 and 8). Such disclosures were discussed in greater detail in Applicant’s previous Response to Office Action dated February 3, 2005; however, the Office has failed to comment as to such disclosures.

Given the “blue-print” of the particular amino acid sequences recited in the claims, the knowledge in the art as to the physical and chemical properties of those and other amino acids, and the additional guidance provided in the specification, the ordinarily-skilled artisan would have immediately recognized that the amino acid sequences recited in the pending claims could be conservatively substituted without eliminating the function of such peptides (Saxinger Declaration at para. 9). Furthermore, such a person could have immediately ascertained such sequences using the disclosures of the specification and the general knowledge available in the art at that time (Saxinger Declaration at para. 9). Thus, the ordinarily-skilled artisan at the relevant time would have appreciated that the Applicant was

in possession of the claimed sequences comprising up to six conservative or neutral amino acid substitutions.

For the foregoing reasons, the subject matter of the pending claims meets the written description requirement of Section 112, first paragraph. Accordingly, this rejection should be withdrawn.

Conclusion

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "John L. Gase", is written over a horizontal line.

John L. Gase, Reg. No. 47,590
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson Avenue
Chicago, Illinois 60601-6780
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

Date: August 2, 2005